REMARKS

Claims 1-58 are currently pending, with claims 1-32, 37, and 50-52 under consideration (claims 33-36, 38-49 and 53-58 having been withdrawn by the Examiner as drawn to non-elected subject matter). Claims 1, 9, 20, 31, and 50 are amended by the present communication. None of the subject amendments introduces new matter as all are supported by the specification at, for example, paragraphs [0023] and [0057], and the claims as originally filed. Upon entry of the present amendment, claims 1-32, 37, and 50-52 will remain pending and at issue.

I. Claim Objections

The Examiner has objected to claim 9 based on containing an alleged informality. In particular, the Examiner asserts that the expression "population of stem *cell or differentiate* into a substantially uniform population" does not make sense and appears to contain a typographical error. Without acquiescing to the reasoning offered by the Examiner, claim 9 has been amended herein to recite "population of stem *cells differentiate* into a substantially uniform population," consistent with the Examiner's suggestion. Accordingly, reconsideration and withdrawal of this objection are respectfully requested.

II. Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-32, 37, and 50-52 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly not enabled by the specification. Applicants traverse the rejection as applied to the claims as presently amended.

The Examiner acknowledges that the specification is enabling for a method for inducing differentiation of an embryonic neural stem cell into a neuron, comprising contacting a stem cell with a Hedgehog protein and β-cyclodextrin (βCD). However, the Examiner asserts that the specification is not enabling for any method that induces any stem cell that produces a substantially uniform population of differentiated neurons, wherein the stem cell is any cell other than an embryonic neural stem cell or that the differentiated neuron is any other than floor plate or motor neurons. Applicants respectfully submit that the specification fully enables the scope of the claims as presently amended.

The specification supplies the novel aspects of the invention, that is, that "contacting a stem or progenitor cell with a sterol-depleting agent and a differentiation signaling agent, results in differentiation of the stem or progenitor cell into a substantially uniform population of differentiated neurons" (specification at paragraph [0005]). In particular, the specification provides that "contact of stem cells and/or progenitor cells with β-cyclodextrin (βCD) and a Hedgehog protein results in differentiation of the stem and/or progenitor cells into a substantially uniform population of differentiated neurons" (specification at paragraph [0005]).

Accordingly, the present invention, as defined by amended claim 1, is directed to a method for inducing differentiation of a stem cell into a neuron, by contacting a stem cell with a Hedgehog protein and β-cyclodextrin (βCD) under conditions sufficient to decrease sterol concentration in the cell, wherein the stem cell is an embryonic stem cell or a neuronal stem cell, thereby inducing the stem cell to differentiate into a neuron.

It is respectfully submitted that the specification provides detailed description of the components utilized in the method, as well as how the method steps may be conducted. For example, a description of the components for use in the claimed methods is provided at, e.g., paragraphs [0021]-[0023] for stem cells or progenitor cells, [0058]-[0061] for hedgehog proteins, and [0068] and [0070]-[0071] for βCD. In addition, guidance is provided as to the method steps (e.g., paragraphs [0035]-[0036] and Example 1) and conditions (e.g., [0028]-[0031] and [0051]-[0055]). Finally, the specification provides a working example of the claimed methods at paragraphs [0105]-[0130].

The Examiner asserts that the claims are broad in scope, based on being allegedly directed to a method for any stem cell that produces a substantially uniform population of differentiated neurons. Applicants submit that the claims are commensurate in scope with the teaching of the specification. However, without acquiescing to the reasoning offered by the Examiner and to expedite prosecution, the claims have been amended herein to indicate that the stem cells are embryonic stem cells or neuronal stem cells. Accordingly, the Examiner's concern in this regard has been rendered moot.

With regard to the Examiner's assertion that the specification is allegedly not enabling for a method producing a substantially uniform population of any type of neuron other than a motor neuron, Applicants respectfully disagree. The specification provides that,

> [while] not intend[ing] to be limited by a particular theory, contact of a population of stem cells with a sterol-depleting agent such as βCD is believed to be useful in methods provided herein because the βCD is believed to bring substantially all, or all of the stem cells and progenitor cells in a culture to a similar state of responsiveness to a Hedgehog protein signal and/or a TGFB signal, thus enhancing the uniformity of a differentiation response upon exposure of the cultured cells to a Hedgehog protein or a TGFβ family member, such as a BMP. The Hh protein or TGFβ family member, such as a BMP, is typically added to the culture medium.

Based on this teaching, the skilled artisan would expect that the methods would be applicable to the generation of those types of neurons whose differentiation is known to involve hedgehog. Indeed, as described in the specification, the role of hedgehog in neuronal differentiation has been demonstrated in the art (e.g., paragraphs [0062]-[0064]). For example, the specification provides that "[i]n explants of intermediate neuroectoderm at spinal cord levels, Shh protein induces floorplate and motor neuron development with distinct concentration thresholds, floor plate at high and motor neurons at lower concentrations," citing several reports from the literature (paragraph [0063], citations omitted). The specification further provides that "[i]n explants taken at midbrain and forebrain levels, Shh also induces the appropriate ventrolateral neuronal cell types, dopaminergic ... and cholinergic ... precursors, respectively, indicating that Shh is a common inducer of ventral specification over the entire length of the CNS" (paragraph [0063], citations omitted). It is respectfully submitted that based on these teachings the skilled artisan would reasonably expect success in producing those types of neuron whose differentiation has been shown in the literature to involve hedgehog.

Based on the foregoing, it is respectfully submitted that the claims are fully enabled by the disclosure. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for allowance, and a notice to that effect is respectfully requested.

The Commissioner is hereby authorized to charge $65.00 to cover a One-Month Extension of Time fee to Deposit Account 07-1896. No other fee is believed to be due in connection with the submission filing of this paper. However, the Commissioner is hereby authorized to charge any other fees associated with this submission, or credit any overpayments, to Deposit Account No. 07-1896.

The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

Respectfully submitted,

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